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Transfusion Therapy and Blood Banking in the Dog and Cat

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INTRODUCTION

The first successful transfusion of blood from one dog to another was first reported in 1665 by Richard Lower. He anastomosed a carotid artery of a donor dog to the jugular vein of an acutely bled recipient. At this time in history, blood was regarded as the essence of life and useful only for its alleged psychic effects. It wasn't until 1818 that whole blood was used for its intrinsic value when a London obstetrician initiated blood replacement therapy for postpartum hemorrhage.^{1,2,3}

As veterinary critical care becomes more and more sophisticated, the advantages of a basic knowledge of transfusion therapy and blood banking are increasingly apparent.

The purpose of this article is to offer current knowledge on: 1) storing blood, 2) selection of donors, 3) blood grouping and crossmatching, 4) blood collection, 5) indications for component transfusions, 6) administration, and 7) complications.

STORED BLOOD

Erythrocyte viability is the major determinant of storage time for erythrocytes in various storage media. Some of the factors that affect the viability of stored blood include: 1) biochemical parameters, 2) storage media, 3) storage temperature, 4) storage container type, 5) frequency of gentle mixing during storage, and 6) collection technique.

Biochemical Parameters

There are several biochemical parameters that correlate with cellular viability during storage. These include intracellular ATP, 2-

3-diphosphoglycerate (2-3-DPG), pH, and ammonia.¹

In human erythrocytes, intracellular ATP decreases during storage. Erythrocytes with decreased ATP levels have rigid cell membranes, resulting in rapid removal from the circulation by the reticuloendothelial system.¹ In addition, ATP, being a phosphoric compound, affects the oxygen dissociation curve.^{6,7} The ATP content may not be as important in cellular viability in dogs as it is in humans.

Another biochemical change that occurs in stored blood is the decrease in 2-3-diphosphoglycerate (2-3-DPG) levels. 2-3-DPG is an organic phosphate substance found in RBC's that facilitates a shift of the oxygen dissociation curve to the right.⁷ As storage time increases, the concentration of 2-3-DPG decreases and the curve shifts to the left (Fig. 1). As a result, hemoglobin releases less oxygen to the tissues for a given partial pressure.^{1,3,8} Because of tremendous restoration capabilities, the recipient is able to restore normal 2-3-DPG levels in the transfused cells within 24 hours. RBC's totally depleted of 2-3-DPG can regain 50% of the normal level within 24 hours.^{1,3}

Blood depleted of 2-3-DPG or blood stored greater than 2 weeks should not be used in a patient requiring large amounts of transfused blood in a short time or a patient particularly sensitive to tissue hypoxia because the animal may deteriorate before 2-3-DPG levels are restored.^{1,7}

Since the normal metabolism of the cells during storage does not cease, they utilize glucose and produce lactic acid resulting in a decrease in pH. The acidity will cause a right shift of the oxygen dissociation curve, increasing the oxygen-unloading ability at the tissue level. Citrate in the various storage media is

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metabolized to an alkaline byproduct within minutes after transfusion and this tends to negate untoward effects of the acid pH of stored blood. Even so, when using blood stored for prolonged periods it may be advisable to include some sodium bicarbonate in the process of transfusion to aid maintenance of homeostasis in the patient.^{1,6}

Another biochemical parameter of stored blood is the increase of ammonia content. No clinically significant side effects of increased ammonia content of stored blood have been seen, although ammonia toxicity may be a problem in patients with reduced hepatic function in which the toxicity is potentiated by hypoxia.

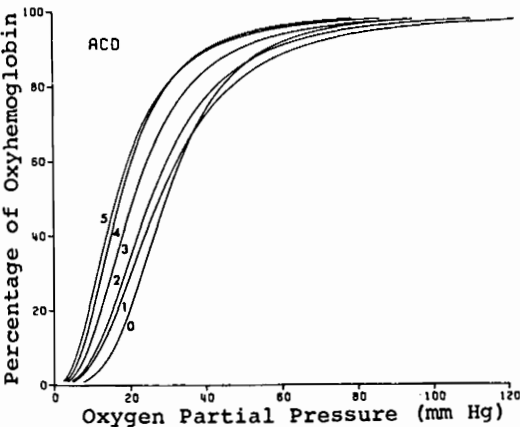


Figure 1. Oxygen Dissociation Curve. The curve shifts to the left during 1,2,3,4,5 weeks of storage.⁸

Storage Media

Various storage media are available to preserve the viability of the erythrocytes and the oxygen-carrying capacity of collected blood. Currently recommended anticoagulants include citrate phosphate dextrose (CPD), citrate phosphate dextrose adenine (CPDA-1), acid citrate dextrose (ACD), storage media for blood (SMB), and heparin.¹

The quantity of citrate in the media is sufficient to bind the ionized calcium present in whole blood, and thus inhibits several steps in the coagulation cascade. The presence of dextrose in the media allows generation of ATP through glycolytic activity. Maintenance of ATP levels correlates with red cell viability. The addition of adenine to the preservative CPDA-1 promotes red cell ATP production and lengthens the shelf-life. Finally, the addition of the phosphoric compounds to blood

helps maintain a normal oxygen dissociation curve.^{6,7}

The storage times of the various media are summarized in Figure 2. Note that heparin has no preservative capabilities.^{1,10} Feline erythrocytes stored in ACD are viable for at least 30 days and retain high erythrocyte viability.^{1,9}

Storage media for blood is similar to ACD but has additional components that keep erythrocytic viability above 70% for 6 weeks. At 6 weeks the oxygen carrying capacity of blood stored in SMB equals that of 2-week-old ACD blood. The SMB is not commercially available. Formulations for SMB and ACD are listed in Table 1.¹⁸

TABLE 1 Formulations for Storage Medium for Blood (SMB) and Acid-Citrate-Dextrose (ACD) Solution.¹⁸

| Factor | SMB | ACD |
|---|-------|------|
| Dextrose (g) | 2.55 | 1.47 |
| Sodium citrate (g) | 2.63 | 1.32 |
| Citric acid (g) | 0.325 | 0.48 |
| Sodium dibasic phosphate (g) | 0.222 | ... |
| Trisodium ascorbate-2-phosphate (g) | 0.406 | ... |
| Water qs (ml) | 100 | 100 |
| pH | 7.0* | 5.0 |
| Milliliters of solution to preserve 100 ml of blood | 17.5 | 25 |

*Adjusted with sodium hydroxide.

Storage Temperatures

Whole blood and packed red cells are stored at 1–6°C to slow glycolytic activity, to avoid rapid depletion of glucose and adenine, and to decrease proliferation of bacteria.⁷ Blood should be thawed slowly at room temperature.

Storage Containers

Three types of containers are used to store blood: glass vacuum bottles, plastic bags, and plastic syringes.¹ Plastic collection bags are preferable to vacuum bottles for four reasons: 1) bags are non-breakable, 2) bags require less storage space before and after collection, 3) gravity-filled bags decrease mechanical trauma to red cells and increase red cell viability, and 4) platelets do not adhere to the walls of plastic bags.^{7,10} A possible disadvantage is the presence of the phthalate ester plas-

ticizer that has been identified in human tissues following transfusion. The significance of this is unknown.⁷ Plastic syringes are used for collection of feline blood.

While blood is being stored, frequent (daily) gentle mixing helps maintain ATP, glucose, and 2-3-DPG levels.^{1,3}

canis, *Hemobartonella canis*, and *Trypanosoma cruzi* should be obtained, depending on the geographical location of the practice. In addition, donors should be free of fleas, ticks, and intestinal parasites (especially hookworms).^{1,2,11}

The requirements for selection of the donor

FIGURE 2 Common Anticoagulants — Preservatives.⁷

| Agent | FDA* Shelf-life of collected blood stored at 1-6°C | Dosage | Comments |
|--|---|---|---|
| Heparin | 24 hours | 250 u heparin/ 50 ml whole blood | No preservative capabilities |
| Acid Citrate Dextrose (ACD) | 21 days | 10 ml ACD/ 60 ml whole blood | 1. Acidic Solution 2. Hypotonic to RBC's so may be removed from circulation earlier. |
| | | Premeasured in commercial administration bags or vacuum bottles | 3. Maintains lower 2-3- DPG levels than other commercially available blood preservatives |
| Citrate Phosphate Dextrose (CPD) | 21 days | same as ACD | 1. Increased % viable cells at 21 days over ACD. |
| Citrate Phosphate Dextrose with Adenine (CPDA-1) | 35 days | same as ACD | 1. Adenine provides substrate for RBC's to synthesize ATP during storage. Results in improved viability. |

*As licensed by FDA. The shelf-life, or maximum allowed storage time, is defined as the expectation that at least 70% of the transfused cells remain in the recipient's circulation 24 hours after transfusion.

SELECTION OF DONORS

The canine donor should be lean, 2-5 years of age, weigh at least 25 kg, be in good physical condition, have a packed cell volume (PCV) of at least 40%, and be adequately immunized. It should not have received prior blood transfusions or had a prior pregnancy. Females should be spayed because of estrogen influences on platelet number and function.^{1,2,11}

Potential donors should be blood typed and vaccinated for distemper, hepatitis, leptospirosis, parainfluenza, and parvovirus. A complete blood count, serum chemistry profile, urinalysis, fecal examination, and a Knotts test should be performed. Serological tests for *Brucella canis* and serum titers for infectious agents such as *Ehrlichia canis*, *Babesia*

cat are similar to those of donor dogs except the donor should be a lean mature 5 kg animal with a PCV greater than 35%. Donor cats should be serologically negative for *Toxoplasma gondii*, *Hemobartonella felis*, feline infectious peritonitis, and feline leukemia.¹

If donors are used repeatedly they need additional dietary supplementation of iron, protein, Vitamin B₁₂, folic acid, and pyridoxine. Meat protein-derived diets ensure an adequate amount of hemoglobin precursors.²

BLOOD GROUPING

Eight specific antigens have been identified on the surface of canine erythrocytes (Table 2). These antigens determine the various blood groups.

The currently accepted acronym for the

canine blood group is DEA (dog erythrocyte antigen).¹ The blood group antigens DEA 1.1 and DEA 1.2 are allelic and never occur on

TABLE 3 Canine Blood Groups¹⁹

| Nomenclature | Common Name | Incidence* |
|--------------|----------------|------------|
| DEA-1.1 | A ₁ | 40 |
| DEA-1.2 | A ₂ | 20 |
| DEA-3 | B | 5 |
| DEA-4 | C | 98 |
| DEA-5 | D | 25 |
| DEA-6 | F | 98 |
| DEA-7 | Tr | 45 |
| DEA-8 | He | 40 |

*In random dog population.

the same red blood cell, but may occur with other canine erythrocyte antigens. All of the blood group antigens are capable of stimulating the formation of specific antibodies (isoantibodies). The group with the greatest potential for antigenic stimulation is DEA 1.1. Reactions to DEA 1.2 are less severe but can be clinically significant. Naturally occurring isoantibodies do not occur against DEA 1.1 or DEA 1.2. However, approximately 15% of the dog population has natural isoantibodies against DEA 3, 4, 5, and 7 with anti-DEA 7 reactions occurring most frequently. As a result, adverse reactions are possible on initial transfusions but rarely occur.^{1,3}

The canine blood donor for a practice should be negative for DEA 1.1 and 1.2. There are several reasons to avoid possible transfusions of DEA 1.1 or DEA 1.2 positive blood into a recipient negative for these antigens: 1) the recipient may produce antibodies and cause delayed hemolysis 7–10 days later; 2) sensitization of the recipient will occur to subsequent transfusion of blood containing DEA 1.1 or DEA 1.2; 3) immediate transfusion reactions in an already sensitized recipient; and 4) the possibility of hemolytic disease of newborn pups that have received isoantibodies from a sensitized dam. For these reasons, it is recommended that canine blood donors be typed negative for DEA 1.1 and DEA 1.2.³

In the feline, there are three specific blood group antigens associated with the erythrocyte membranes. The most common blood group reported was Type A with a 73% occurrence. Type B was found in 26% and Type AB in less than 1% of the cat population.^{1,12} The value of blood typing a feline donor is un-

known at this time. But, since naturally occurring antibodies against other blood types may exist in the cat and antibody production occurs after exposure to a different blood type, crossmatching before all transfusions in the cat is advisable. Blood typing is available through Stormont Laboratories, 1237 E. Beamer St., Woodland, CA 95695.

CROSSMATCHING

The best alternative to blood typing is crossmatching the donor and recipient blood. The use of crossmatched blood does not prevent sensitization of the recipient for future transfusions if the donor cells contained non-identical alloantigens.¹⁵

Two types of crossmatching are performed, major and minor. The major crossmatch uses donor cells and recipient serum and determines whether the recipient has antibodies against the donor cells. The minor crossmatch uses recipient cells and donor serum which detect whether there are antibodies in the donor serum against the recipient cells. Both tests should be performed on fresh blood.¹⁵ Donor and recipient controls are set up along with the major and minor crossmatch.

COLLECTION

Various sites of collection in the dog and cat include: 1) cephalic veins, 2) jugular veins, 3) cardiac ventricles, 4) femoral arteries, and 5) carotid arteries.^{1,10}

Of the various collection sites for the dog, the femoral artery is least traumatic to red blood cells and platelets.³

If syringes are being used or mechanical vacuum equipment is available for plastic bag collection, the jugular vein is preferred because of its size and access.^{1,5}

The animal should be anesthetized and the collection site should be surgically prepared so that strict aseptic technique may be followed.^{1,7} Blood collection should be rapid, uninterrupted and performed through a single puncture site to prevent blood cell damage and the activation of coagulation factors.³ When using the femoral artery, pressure should be applied over the vessel for 5–10 minutes to control hemorrhage.¹ Blood and anticoagulant should be gently mixed during the collection process to prevent clots from forming. The amount of blood that can be withdrawn safely from a dog is about 22ml/kg

(10 ml/lb) of body weight every 7–10 days. A cat can donate this amount safely every 10 days. On an emergency basis, additional blood can be taken after a 5 day recovery period. If the erythrocytes are infused back into the donor following the harvesting of plasma, blood can be collected every two days.¹

By withdrawing 22 ml/kg, a 20 kg dog can yield one unit of whole blood per collection. A unit consists of 450 ml of blood collected into a plastic bag containing 63 ml of the anticoagulant and preservative.¹⁶ Where large volumes are required, it has been suggested to collect from normal patients being euthanized. Permission should be obtained from the owners.¹⁰ Complete exsanguination of a 25 kg dog yields an average of 1000 ml of blood and a 5 kg cat yields an average of 150 ml of blood.¹ The quantity of blood needed for transfusion can be calculated from the equation in Figure 3. The recipient's clinical signs and physiologic status must also be considered.

volume expansion. If coagulation factors and platelets are needed, blood should be used within 8–12 hours after collection because the viability of these components is rapidly lost.¹⁵

Surgical Patient

It is recommended that surgical candidates have a minimum PCV of 27–30%. During surgery the PCV should be maintained above 20%. When possible, transfusions should be given at least 48 hours prior to surgery. Packed red cells are the treatment of choice if serum protein values are normal. During surgery, if blood loss is great, whole blood transfusion or autotransfusion may be indicated.^{3,15}

Anemia

In anemia of hemorrhage or hemorrhagic shock, replacement of blood volume is of primary importance. PCV in the first 8–12 hours posthemorrhage is not an accurate indicator of the extent of hemorrhage. The PCV will not reflect the loss of blood until fluids are

FIGURE 3 Calculation of donor blood volume required.¹⁹

$$\text{Volume of blood required (ml)} = \left[\frac{\text{recipient wt. (kg)}}{\text{kg}} \times 70 \text{ (ml/kg)} \right] \times \frac{\text{Hb rise wanted (gm/dl)}}{\text{donor's Hb (gm/dl)}}$$

INDICATIONS FOR WHOLE BLOOD AND BLOOD COMPONENT TRANSFUSION THERAPY

Separating whole blood into its various components is the most efficient way to use blood or blood products.¹⁵ The various components used include: 1) packed red blood cells, 2) plasma, 3) fresh frozen plasma, 4) cryoprecipitate plasma, 5) platelet-rich plasma, 6) plasma derivatives, and 7) leukocytes.^{7,15}

Indications for whole blood transfusions are: hemorrhage (including bleeding disorders), hemorrhagic shock, nonregenerative anemia, and hemolytic anemias. In anemic conditions that can be treated with packed red cells or iron, whole blood is not necessary unless the anemia is severe enough to be life threatening.¹⁵

Whole blood provides a source of erythrocytes for carrying oxygen to the tissues and it supplies plasma proteins necessary for oncotic

pulled into the vascular space diluting the erythrocytes. Therefore, crystalloid solutions such as Lactated Ringers Solution are suggested for the initial replacement of blood volume.¹

If the PCV falls acutely to 20–25% and adequate hydration has been accomplished, whole blood should be given at a rate of 13–22 ml/kg of body weight. This can be repeated once or twice during the first 24 hours until stabilization of the PCV above 20%.¹

A more specific guideline for the quantity of blood necessary to elevate the packed cell volume to a desired level is shown in Figure 5.

Transfusions are rarely indicated for regenerative anemias but may be indicated for chronic nonregenerative nonhemolytic anemias. Many animals with a chronic anemia have 2–3-DPG levels two to three times normal and their oxygen transport and delivery is adequate. The patient should have clinical signs of anemic anoxia such as anorexia, ex-

cessive weakness, orthopnea, or edema before therapy is initiated.³ The PCV necessitating the administration of transfusion therapy is variable for chronic nonregenerative anemia.^{1,3} When the PCV is less than 10% in chronic anemia, transfusion may be indicated.³ Another source establishes the PCV at 15% for the dog and 12% for the cat.¹

In autoimmune hemolytic anemia, transfusions should be used only as a life saving measure because they can accelerate hemolysis.^{1,3}

Transfusions may be indicated in non-autoimmune hemolytic anemias associated with diseases such as Heinz-body anemias in cats and onion poisoning in dogs if the PCV falls to a life-threatening level.¹

Packed red cells are specifically indicated in patients that require improved oxygen carrying capacity but do not require volume replacements.¹⁶

Hypoproteinemia

Hypoproteinemia exists when there is a normal hematocrit and the total plasma protein is less than 5g/dl.^{1,2} Protein replacement therapy may be indicated if the albumin levels are less than 1.5 g/dl.^{1,2} Fresh or frozen plasma should be transfused at a rate of 6–12 ml/kg body weight. The frequency of plasma administration depends on the protein deficit and ongoing loss.¹ There is a danger of volume overload with the use of whole-blood transfusion for the treatment of hypoproteinemia.¹ Harvested plasma can be stored at –40° to –70°C for up to one year or in a household freezer for 3 months.¹⁵

COAGULOPATHIES

Disseminated Intravascular Coagulation

There is considerable controversy over the treatment of this condition. Currently mild DIC is treated with heparin or aspirin. Severe DIC is treated with heparin and replacement of clotting factors with fresh whole blood or fresh plasma.¹ Other sources say fresh whole blood is the treatment of choice in the actively bleeding DIC patient.³

Thrombocytopenia

The underlying cause of thrombocytopenia should be identified and treated if possible. Fresh whole blood may be administered but it should be noted that large volumes of blood

are necessary to significantly elevate the recipient's thrombocyte count. Platelet-rich plasma is superior to whole blood in treating thrombocyte disorders. Harvesting platelet-rich plasma has been described.¹⁵

Congenital or Acquired Factor and Vitamin K Deficiencies

For both hereditary and acquired causes of bleeding disorders, whole blood, plasma, or plasma components can be administered. Cryoprecipitates are used to treat inherited bleeding disorders and are rich in the antihemophilic factor, Von Willebrand's factor, and fibrinogen. Actions of factors IX, XI, and XIII are also exhibited.¹⁵

Vitamin K therapy may be all that is needed if Vitamin K deficiency is suspected such as in warfarin-related poisonings.¹

Liver Disease

The liver is the primary site of production of plasma procoagulants and numerous hemostatic defects may be present in liver disease. Whole blood or, preferably, fresh plasma can be given to patients with severe liver disease.¹

BLOOD ADMINISTRATION

Blood should be administered through a filter system to minimize transfusion of microaggregates of platelets, white blood cells, fat, and emboli that may occur due to poor collection techniques.^{7,3}

Blood should be warmed to 37°C to avoid hypothermia. Excessive heat should not be used to accelerate blood warming because fibrinogen precipitates and red blood cells hemolyze if warmed to 50° C. Autoagglutination occurs when temperatures exceed 45° C.^{15,3}

Blood is most commonly administered via the cephalic or jugular veins. Neonatal canine and feline patients can be infused into the medullary cavity of the femur or humerus. Systemic absorption of blood infused into the medullary cavity is rapid, 95.3% within five minutes. Blood can also be infused into the patients peritoneal cavity.^{15,16} The disadvantages of the latter two techniques include: 1) decreased numbers of viable red cells that enter the recipients circulatory system, 2) decreased life span of the transfused erythrocytes, 3) pain, and 4) possibility of introducing peritonitis or osteomyelitis.^{15,16}

An initial intravenous transfusion rate of 0.25 ml/kg over a 30-minute period is suggested during which the patient should be watched carefully for transfusion reactions.¹⁵

The recommended transfusion rate of whole blood in dogs is less than 22 ml/kg/day. A hypovolemic patient may receive up to 22 ml/kg/hour. Dogs in cardiac failure cannot tolerate rates exceeding 4 ml/kg/hour.¹⁵

In an adult cat weighing 2–3 kg, up to 40 ml of whole blood can be given intravenously over a 30-minute period. The safest technique is frequent infusion of small amounts of blood.¹⁵

Crystalloid solutions may be administered simultaneously with whole blood, packed red cells, or plasma to aid in correction of hypovolemia and restoration of cardiac output. However, only normal saline or balanced electrolyte solutions without calcium should be administered through the same catheter. Solutions containing calcium, such as Lactated Ringers, should be administered using separate tubes because of the possibility of clotting within a common tube. Dextrose solution may cause autoagglutination, hemolysis or both.^{1,3,16}

COMPLICATIONS

Blood transfusions can produce various adverse reactions. The most effective means of decreasing the incidence of transfusion reactions is to avoid transfusion therapy unless it is absolutely indicated.^{15,16}

Transfusion reactions can be divided into immunologically and nonimmunologically mediated reactions. These are summarized in Figure 4.

Nonimmunologically mediated transfusion reactions include vascular overload and fever. Vascular overload may result in clinical signs of dyspnea, cough, and vomiting. Nonimmunologic fever results from break in aseptic technique during collection, administration, or storage of blood.^{15,16}

The most severe transfusion reactions are immunologically mediated hemolytic reactions. Severe transfusion reactions in both the dog and cat may begin within seconds to minutes.^{12,17}

In immediate onset hemolysis, the transfusion should be stopped immediately and saline given intravenously. Shock treatment may be necessary. Despite the apparent severity of acute hemolytic reactions, they are usu-

ally not fatal. The patient typically is fully recovered in 12 to 24 hours.¹⁵

It is important to carefully monitor the patient during transfusion therapy and follow the guidelines for proper administration of blood components.

FIGURE 4 Summary of Transfusion Complications.

Summary of Nonimmunologic Reactions to Transfusion.

- A. Vascular Overload
 - 1. Cough
 - 2. Dyspnea
 - 3. Vomiting
- B. Fever
- C. Asymptomatic Hemolysis
 - 1. Physical trauma to red blood cells
 - a. Freezing
 - b. Overheating
 - c. Mixing red cells with nonisotonic solutions

Summary of Immediate Immunologic Reactions

- A. Hemolysis Due to Red Cell Incompatibility
 - 1. Restlessness and anxiety
 - 2. Urticaria/pruritus
 - 3. Muscle tremors
 - 4. Nausea/salivation/vomiting
 - 5. Fever
 - 6. Apnea and/or tachypnea
 - 7. Tachycardia
 - 8. Fecal and/or urinary incontinence
 - 9. Anuria/renal failure
 - 10. Convulsions
- B. Nonhemolytic Reactions
 - 1. Urticaria/pruritus usually due to antibody to plasma protein
 - 2. Anaphylaxis due to antibody to IgA
 - 3. Fever due to antibody to leukocytes

Summary of Delayed Immunologic Reactions

- A. Hemolysis due to anamnestic antibody to cell antigen
 - 1. Clinical signs similar to immediate immunologic reactions but usually not as profound
 - 2. Drop in PCV 2–21 days post-transfusion
- B. Delayed phagocytosis approximately 7–10 days post-incompatible transfusion due to antibody formation
- C. Post-transfusion purpura due to antiplatelet antibodies

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